

**PACKAGING FOR IMPARTING ANTI-MICROBIAL PROPERTIES
TO A MEDICAL DEVICE**

FIELD OF THE INVENTION

[001] This invention is generally directed to the imparting of anti-microbial properties to medical devices, and more particularly to the use of medical device packaging as a way to impart anti-microbial properties to medical devices.

BACKGROUND OF THE INVENTION

[002] Despite the advances in sterilization, infections resulting from the use of medical devices continue to pose a problem. Even if a medical device has been properly sterilized before use, mere sterilization does not prevent a medical device from subsequently becoming re-contaminated by disease-causing microbes. For example, the surface of medical devices, such as catheters, that remain partially implanted within the body can become re-contaminated after the initial implantation by infectious microbes that travel through the air. The microbes can then grow on the surface of the medical device and eventually enter the body through the entry site of the medical device into the body, resulting in infection. Re-sterilization of the device after implantation, even when feasible, is difficult and time-consuming.

[003] Therefore, it has been found that in addition to sterilizing medical devices before use, it is desirable to also impart anti-microbial properties to the surface of the medical devices, particularly for those medical devices, such as catheters, that remain partially inserted in the body for a substantial period of time. By preventing the growth of microbes on the surface of medical devices after implantation, infections may be further reduced.

[004] Providing the surfaces of medical devices with anti-microbial properties is known in the art. Current methods used to impart anti-microbial agents onto medical devices included coating or co-extruding the surface of the medical device with an anti-microbial agent. However, these methods often require a change in the manufacturing process of the medical device, which may be difficult, costly and/or impractical. Furthermore, if the medical device is to be stored for a long time prior to use, there may be a degradation of the effectiveness of an anti-microbial coating on the medical device.

[005] The present invention teaches a novel method of imparting anti-microbial agents onto medical devices by using certain packaging advantages.

SUMMARY OF THE INVENTION

[006] In a first embodiment, a system for packaging a medical device comprises a container with a first compartment and a second compartment, the first compartment being configured and adapted to house the medical device, and the second compartment being configured and adapted for containing an anti-microbial agent. A partition between the first compartment and the second compartment prevents fluid communication between the first compartment and the second compartment, with at least part of the partition being removable or breakable to allow fluid communication between the first compartment and the second compartment.

[007] In a further embodiment, the partition further comprises an opening and a sealing element covering said opening. The sealing element may be removable from the opening. The sealing elements may be removed by peeling the sealing element from the opening. Alternatively, the partition may further comprise a removable member attached to the partition, wherein removal of the removable member results in a tearing of the partition.

[008] In yet another embodiment, a cover is capable of being disposed over the container. The removable or breakable part of the partition may be connected to the cover.

[009] The anti-microbial agent may be selected from iodine, hypohalites, haloamines, thiocyanogen, hypothiocyanite, silver ions, triclosan, penicillin, amoxycillin, rapromycin, or combinations thereof. The anti-microbial agent may be a fluid or a gel.

[010] In another preferred embodiment of the present invention, a method for imparting anti-microbial properties to a medical device comprises the steps of (a) obtaining a container comprising a sealable first compartment configured and adapted to house the medical device, a sealable second compartment configured and adapted to store an anti-microbial agent, and a partition between the first compartment and the second compartment to prevent fluid communication between the first compartment and the second compartment, wherein at least part of the partition being breakable or removable to allow fluid communication between the first compartment and the second compartment; (b) filling the second compartment with an anti-microbial agent; (c) placing a medical device in the first compartment; (d) sealing the first and second compartments; and (e) removing or breaking at least part of the partition to allow fluid communication between the first and the second compartments to allow the anti-microbial agent to flow from the second

compartment into the first compartment. The method may further comprise allowing the anti-microbial agent to coat the medical device.

[011] In a further embodiment, the container further comprises a cover capable of being disposed over the container, and the removable or breakable part of the partition is connected to the cover; and the step of removing the removable part of the partition is accomplished by removing the cover from the container.

[012] In another preferred embodiment, the system for packaging a medical device having a lumen, comprises a pouch comprising an interior surface and a first anti-microbial agent; a tray disposed within the pouch; and a substrate attached to the tray; wherein the substrate comprises a second anti-microbial agent and wherein the substrate is capable of being inserted into the lumen. The first anti-microbial agent may be disposed on the interior surface of the pouch. In a preferred embodiment, the substrate is in the form of a rod, and may be formed of an iodine-polycarbonate material. In another preferred embodiment, the substrate may be coated with the second anti-microbial agent. The first and the second anti-microbial agents may be the same. The pouch may further comprise a sealable opening.

[013] In a further embodiment, the system further comprises a cylinder comprising a third anti-microbial agent, wherein the cylinder is disposed around the tray and within the pouch. The third anti-microbial agent may be the same as the first and second anti-microbial agents. The cylinder may be formed from the third anti-microbial agent. In another preferred embodiment, the third anti-microbial agent is coated onto the cylinder.

[014] In another preferred method for imparting anti-microbial properties to a medical device having a lumen, the method may comprise the steps of (a) obtaining a container comprising a pouch having an interior surface, a tray disposed within the pouch, and a substrate attached to the tray, wherein the interior surface of the pouch comprises a first anti-microbial agent, and the substrate comprises a second anti-microbial agent; (b) inserting the substrate into the lumen; and (c) inserting the tray in to the pouch. The method may further comprise the step of sealing the pouch. The lumen may be filled with an aqueous solution, wherein the aqueous solution serves as a release medium for the second anti-microbial agent. The first and the second anti-microbial agents may be the same.

[015] The present invention allows for the imparting of anti-microbial agents to medical devices without otherwise changing the characteristics or materials of the medical devices. Furthermore, the present invention allows anti-microbial agents to be imparted to medical devices without changing the manufacturing process for the medical device. Also, the present invention allows the anti-microbial agent to be imparted to the medical device

shortly before used of the medical device, thereby avoiding potential degradation of the effectiveness of the anti-microbial agent.

BRIEF DESCRIPTION OF THE DRAWINGS

[016] **Fig. 1** is a perspective view of an embodiment of the present invention with the cover removed.

[017] **Fig. 2** is a cross-sectional view of the embodiment of **Fig. 1**.

[018] **Figs. 2A** and **2B** are side views of the partition of the embodiment of **Fig. 1**. **Fig. 2A** illustrates a zip strip secured to the partition, while **Fig. 2B** illustrates the zip-strip being partially removed from the partition.

[019] **Figs. 3A** and **3b** are side views of another embodiment of a zip strip and a partition. **Fig. 3A** illustrates the zip strip secured to the partition, while **Fig. 3B** illustrates the zip-strip that is attached to a portion of the partition being partially torn away from the remainder of the partition.

[020] **Fig. 4** is a perspective view of another embodiment of the present invention.

[021] **Fig. 5** is a perspective view of yet another embodiment of the present invention.

[022] **Fig. 6** is a perspective view of yet a further embodiment of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[023] In a preferred embodiment, as shown in **Figs. 1** and **2**, package **100** generally comprises container **101** with bottom **102**, open top **103**, and removable cover **140** that is capable of being disposed over the container. Partition **130** separates the interior of container **101** into first compartment **110** and second compartment **120**. The partition **130** prevents the first compartment from being in fluid communication with the second compartment. First compartment **110** is configured and adapted to hold medical device **200**. Second compartment **120** is configured and adapted to hold an anti-microbial agent **210**.

[024] Container **101** may be made of various materials. Suitable materials include without limitation polyurethane and its copolymers, silicone and its copolymers, ethylene vinyl-acetate, polyethylene terephthalate, thermoplastic elastomers, polyvinyl chloride, polyolefins, cellulose, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, polycarbonates, acrylonitrile butadiene styrene copolymers, acrylics, polylactic acid, polyglycolic acid, polycaprolactone, polylactic acid-polyethylene oxide copolymers,

cellulose, collagens, and chitins. Preferred materials include, but are not limited to, polyethylene terephthalate, polypropylene, polystyrene, polyethylene, and polyurethane.

[025] The partition can be made of material that is the same as or different from the container material. Preferably the material used to make the partition is a polymeric material.

[026] Suitable anti-microbial agents include, but are not limited to, elemental iodine (also called free iodine), hypohalites, haloamines, thiocyanogen, hypothiocyanite, silver ions, triclosan, antibiotics such as penicillin and amoxycillin, and rapromycin. Preferably the anti-microbial agent 210 is in gel or fluid or liquid form. Agent 210 may also be in a gaseous form.

[027] Partition 130 separates first compartment 110 and second compartment 120. When partition 130 is broken or removed, first compartment 110 and second compartment 120 are in fluid-communication with one another. In a preferred embodiment, partition 130 is formed with partition opening 131 (as shown in Fig. 2A), which is sealed or covered by removable sealing member or “zip-strip” 132. Removal of zip-strip 132 allows anti-microbial agent 210 to flow from second compartment 120 into first compartment 110 through opening 131. Zip strip 132 may be removed by peeling it from partition 130. In the embodiment shown in Fig. 2B, opening 132 is a slit that is formed along a diagonal of partition 130. However, opening 132 may take on many different configurations and still be within the spirit and scope of the invention. Preferably, opening 131 is configured such that at least a portion of partition wall 130 near bottom 102 will be compromised when zip-strip 132 is removed, to allow for all of anti-microbial agent 210 to flow from second compartment 120 to first compartment 110. Therefore, it is preferable that opening 131 ends at or proximate to the bottom 131 of container 101.

[028] Zip strip 132 may be connected to cover 140 by attaching tab 134 to cover 140. In this configuration, removal of cover 140 from container 101 will simultaneously remove zip-strip 132 from opening 131 (as shown in Fig. 2B). The skilled artisan is aware of methods suitable for attaching tab 134 to cover 140.

[029] It is readily seen that the invention may be practiced by several different configurations of the partition 130 and zip-strip 132, so long as the removal of zip strip 132 results in fluid- or flow-communication being established between first compartment 110 and second compartment 120. For example, in an alternative embodiment, as shown in Figs. 3A and 3B, partition 130a does not have an opening, but rather is composed of a material that is easily breakable or torn. Zip strip 132a is adhesively attached to partition 130a. Removal of zip strip 132a by pulling on tab 134a results in the tearing of partition

130a, thus establishing flow-communication between first compartment **110** and second compartment **120**. Preferably, in this embodiment zip-strip **132a** is more resistant to tearing than partition **130a**, so that zip-strip **132a** will not break as partition **130a** is being torn.

[030] Package **100** is prepared for use by first sterilizing first and second compartments **110** and **120** of container **101**. Second compartment **120** is then filled with anti-microbial agent **210**, and medical device **200** is placed into first compartment **110**. Cover **140** is then placed over the top of container **101** and partition wall **130**, sealing first compartment **110** and second compartment **120**. In certain embodiments, tab **134** of zip-strip **132** is attached or connected to cover **140**. Preferably, cover **140** is attached to container **101** so that first compartment **110** and second compartment **120** are hermetically sealed, to prevent microbes from entering and contaminating medical device **200** and/or exposing anti-microbial agent **210** to the environment, which may cause degradation of the effectiveness of anti-microbial agent **210**. Package **100** may then be stored until medical device **200** is needed.

[031] When medical device **200** is needed, the user opens container **101** by removing cover **140**. Zip-strip **132**, if attached to cover **140**, is simultaneously removed from opening **131**. Otherwise, zip-strip **132** is removed after cover **140** is removed. Second compartment **120** and first compartment **110** are now in fluid- or flow-communication with each other through opening **131**, allowing anti-microbial agent **210** to flow from second compartment **120** into first compartment **110** to impart anti-microbial properties to the surface of medical device **200**. Preferably, the anti-microbial agent coats or bathes the medical device. Once a sufficient amount of time has elapsed, the user may then remove medical device **200** from first compartment **110**. To ensure that all parts of medical device **200** are exposed to the anti-microbial agent **210** and to facilitate the flow of anti-microbial agent **200** from second compartment **120** to first compartment **110**, the user may shake or tilt container **101** accordingly.

[032] It is readily appreciated that medical device **200** does not have to be modified in any way in order to be stored within packaging embodying the present invention. Thus, anti-microbial properties may be provided to medical device **200** without modifying medical device **200** or its manufacturing process.

[033] Packaging that embodies the present invention is preferable to having an anti-microbial agent that is stored and applied separately by the user. For instance, by connecting zip-strip **132** to cover **140**, exposure of the medical device **200** to the anti-microbial agent **210** occurs automatically once cover **140** is removed from container **101**, providing a safeguard against inadvertently forgetting to treat medical device **200** with anti-

microbial agent **210**. Because a sufficient amount of anti-microbial agent **210** is packaged with medical device **200**, the danger of using too little or too much of anti-microbial agent **210** is also minimized. Furthermore, because anti-microbial agent **210** is stored in a hermetic environment, any environmentally caused degradation of the anti-microbial agent is reduced.

[034] Another advantage is that one anti-microbial agent **210** is readily interchangeable with other anti-microbial agents, even if their physical properties, such as weight and viscosity, differed greatly. Thus, the potential difficulties of modifying a manufacturing technique for a medical device are avoided.

[035] Many modifications and alternative embodiments of the above concepts may be utilized while remaining within the spirit and scope of the present invention. For example, in another preferred embodiment, zip strip **132** is not attached to cover **140** by tab **134**. This embodiment allows the user to delay the exposure of the medical device to the anti-microbial agent until after the cover has been opened. In yet another preferred embodiment, separate covers may be provided for first compartment **110** and second compartment **120**. This embodiment allows anti-microbial agent **210** and medical device **200** to be sealed into their respective compartments at different times in the manufacturing/packaging process.

[036] Furthermore, many different configurations of the container and the two compartments may be used within the spirit and scope of the present invention. For example, in the preferred embodiment illustrated in Fig. 4, container **301** is generally in the form of a tube which is configured and adapted to house medical device **200**. Attached to the top of container **301** is a compartment for housing the anti-microbial agent that is in the form of a gel-pack **310**, which is composed of a readily torn material. The gel pack **310** is filled with anti-microbial agent **210** and is situated directly over medical device **200**. The zip strip **320** is attached to the gel pack **310** and to the cover **340** via a string **321**. Removal of cover **340** from container **301** tears zip strip **320** from gel pack **310**, opening gel pack **310** and allowing anti-microbial agent **210** to spill onto medical device **200**. Alternatively, the zip-strip may not be attached to the cover, so that the cover must first be removed before the zip-strip is removed.

[037] Medical device **200** may be any of a number of devices, including scalpels, retractors, clamps, catheters, suture needles, and other medical devices.

[038] Another method of using packaging to impart anti-microbial properties to a medical device is to treat components of the packaging with anti-microbial agents. The

components of the packaging would then transfer the anti-microbial agents to the medical device, preferably via diffusion.

[039] Fig. 5 illustrates a preferred embodiment of the present invention. Package 400 comprises a pouch 401 and a tray 410. Pouch 401 further comprises sealable opening 402 and interior surface 403. Interior surface 403 is treated with a first anti-microbial agent 501. This can be accomplished in a number of ways. For example, interior surface 403 may be coated with first anti-microbial agent 501. Interior surface 403 may also have first anti-microbial agent 501 embedded within it. First anti-microbial agent 501 may also be integrally mixed into the material that composes interior surface 403.

[040] Suitable anti-microbial agents include, but are not limited to, elemental iodine (also called free iodine), hypohalites, haloamines, thiocyanogen, hypothiocyanite, silver ions, triclosan, antibiotics such as penicillin and amoxycillin, and rapromycin.

[041] Tray 410 generally comprises bottom 411, open top 412, tray walls 413, and substrate 420. Substrate 420 has distal end 422 and proximal end, 424 and is attached to base 426. Base 426 is attached to tray 410. In a preferred embodiment, base 426 is removable from tray 410. Substrate 420 is configured and adapted to fit inside medical device 200 with interior surfaces that may be exposed to a patient, *e.g.*, a lumen of a medical device. For example, medical device 200 may be a catheter with a lumen, and substrate 420 may be in the form of a rod that is insertable into the lumen.

[042] It is preferred that pouch 401 is manufactured from a material that can prevent the migration of iodine or other anti-microbial agents through pouch 401. Suitable materials include without limitation polyurethane and its copolymers, silicone and its copolymers, ethylene vinyl-acetate, polyethylene terephthalate, thermoplastic elastomers, polyvinyl chloride, polyolefins, cellulotics, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, polycarbonates, acrylonitrile butadiene styrene copolymers, acrylics, polylactic acid, polyglycolic acid, polycaprolactone, polylactic acid-polyethylene oxide copolymers, cellulose, collagens, and chitins. Preferred materials include, but are not limited to, polyethylene terephthalate, polypropylene, polystyrene, polyethylene, and polyurethane.

[043] Substrate 420 can be formed from a second anti-microbial agent 502 that may be the same or different from the first anti-microbial agent 501. In a preferred embodiment, substrate 420 may be made of an iodine-polycarbonate material. Alternatively, the substrate 420 can be formed from a material that does not contain an anti-microbial agent. The anti-microbial agent is then coated onto the substrate. For example, suitable materials for forming the substrate include a polymer that is biodegradable or non-biodegradable. In

addition, the polymer that may be hydrophilic or hydrophobic, and may be selected from the group of polycarboxylic acids, cellulosic polymers, including cellulose acetate and cellulose nitrate, gelatin, polyvinylpyrrolidone, cross-linked polyvinylpyrrolidone, polyanhydrides including maleic anhydride polymers, polyamides, polyvinyl alcohols, copolymers of vinyl monomers such as EVA, polyvinyl ethers, polyvinyl aromatics, polyethylene oxides, glycosaminoglycans, polysaccharides, polyesters including polyethylene terephthalate, polyacrylamides, polyethers, polyether sulfone, polycarbonate, polyalkylenes including polypropylene, polyethylene and high molecular weight polyethylene, halogenated polyalkylenes including polytetrafluoroethylene, polyurethanes, polyorthoesters, proteins, polypeptides, silicones, siloxane polymers, polylactic acid, polyglycolic acid, polycaprolactone, polyhydroxybutyrate valerate and blends and copolymers thereof as well as other biodegradable, bioabsorbable and biostable polymers and copolymers. Coatings from polymer dispersions such as polyurethane dispersions (BAYHDROL®, etc.) and acrylic latex dispersions are also within the scope of the present invention. The polymer may be a protein polymer, fibrin, collagen and derivatives thereof, polysaccharides such as celluloses, starches, dextrans, alginates and derivatives of these polysaccharides, an extracellular matrix component, hyaluronic acid, or another biologic agent or a suitable mixture of any of these, for example.

[044] Preferred materials for the substrate **420** include, but are not limited to, polyurethane, polycarbonate, silicone, ethyl vinyl acetate, polypropylene, polyamides, polyimides, PEBAX or similar material, and co-polymers thereof. The material may be biodegradable or non-biodegradable.

[045] The amount of second anti-microbial agent **502** may be varied according to the desired effect. The manufacture of the substrate **420** and the use of the substrate **420** for providing anti-microbial activity is described in WO 00/74743 A1.

[046] An aqueous solution may also be contained in the lumen of the catheter or medical device **200**. The aqueous solution may be any solution that can serve as a release medium for the second anti-microbial agent **502** from the substrate. Suitable solutions include, but are not limited to, saline, heparin, and sterile water. Once the substrate **420** is positioned in the lumen, the substrate **420** is exposed to the aqueous solution. The aqueous solution allows the second anti-microbial agent **502**, such as iodine, to migrate from the substrate **420** and enter the liquid phase. By egressing from the substrate **420** and entering the liquid phase in the aqueous solution, second anti-microbial agent **502** can proliferate along the entire length of the lumen to provide anti-infection activity. The lumen does not have to contain an aqueous solution, in which case the second anti-microbial agent **502**

would egress from the substrate **420** and impart anti-microbial properties to the lumen of the medical device **200**.

[047] Medical device **200**, after being sterilized, is placed in tray **410**, with substrate **420** being inserted into a lumen or other interior compartment of medical device **200** that is to be treated. Tray **410** is then inserted into pouch **401** and opening **402** is sealed. Second anti-microbial agent **502** is released from interior surface **403** and substrate **420** onto the exterior and interior surfaces of medical device **200** respectively. It is readily seen that no modifications of medical device **200** need to be made.

[048] It is noted that certain types of anti-microbial agents may need humidity and/or elevated temperatures within package **400** to facilitate diffusion of the anti-microbial agent onto the surface of medical device **200**.

[049] In an alternative embodiment, as shown in **Fig. 6**, package comprises pouch **400**, cylinder **450**, and tray **410**. In this embodiment, interior surface **451** of cylinder **450** is treated with a third anti-microbial agent **503** instead of or in addition to interior surface **403** of pouch **401**. This embodiment may be used if there is difficulty in providing the interior surface **403** of pouch **401** with anti-microbial agent **501**. It may be easier to provide interior surface **451** of cylinder **450** with third anti-microbial agent **503**, as cylinder **450** may be composed of the same material as rod **410**. In this embodiment, substrate **420** is inserted into medical device **200**, and then tray is inserted into cylinder **450**. Cylinder **450** and tray **410** are then sealed within pouch **401**. Substrate **420** imparts the second anti-microbial agent **502** to the interior surfaces of medical device **200**, while cylinder **450** imparts third anti-microbial agent **503** to the exterior surfaces of medical device **200**. The first, second, or third anti-microbial agents may be the same or different.

[050] It is readily seen that many different modifications can be made to the package as described above without departing from the spirit and scope of the present invention. For example, multiple rods may be provided to treat the interior surfaces of a medical device with multiple lumens or interior compartments. Instead of a pouch made of a flexible material, a container made of a rigid material may be used. All references cited herein are incorporated by reference in their entirety for all purposes.